## ATTACHMENT A

Clean Replacement Paragraphs

*At the following locations, replace the previously provided paragraph with the following clean paragraph(s).*

*Page 10, lines 1-17.*

In accordance with the present invention, it is preferred to obtain a serum albumin having a truncation or deletion especially at the three flexible residues on the n-terminus, namely the **Asp-Ala-His** residues which are connected to the sequence Lys-Ser-Glu at the n-terminal region. In a particularly preferred embodiment of the invention, the desired albumin sequence will have a single amino acid truncation which removes the **Asp** residue at the n-terminal end and which will thus have the sequence **Ala-His**-Lys-Ser-Glu (SEQ ID NO: 1). . . This embodiment is particularly preferred because it is least likely to produce an antigenic response yet should significantly reduce trace metal binding at the n-terminal end. Similarly, deletions or truncations of a size greater than a single amino acid are also contemplated by the invention, and will also result in an improved albumin which is less likely to bind to metals such as copper and nickel. Accordingly, other n-terminal deletions in the region of the three flexible residues at the n-terminal end are also suitable in the invention, and thus n-terminal sequences such as His-Lys-Ser-Glu (SEQ ID NO: 2). . . and Lys-Ser-Glu. . . will also be useful in the modified albumin of the invention. Additionally, any other further truncation of the n-terminal end that is sufficient so as to either sterically hinder the binding site VI or eliminate vital binding interactions at that region will be suitable as a modified albumin in accordance with the invention.

*[Page 10, line 18 to Page 11, line 2.]*

In addition, other suitable forms of the present invention will include those additions or substitutions of the amino acid sequence at the n-terminal region or the binding site VI which are sufficient to disrupt the binding of trace metals such as copper and nickel to the albumin, either by providing sufficient steric hindrance to inhibit metal binding or by disrupting or eliminating vital binding interactions. For example, any suitable leader sequence or other elongation at the n-terminal sequence **Asp-Ala-His**-Lys-Ser-Glu (SEQ ID NO: 3). . . will be useful to provide a modified albumin in accordance with the invention.

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*[Page 11, lines 3-12.]*

Furthermore, in another preferred embodiment in accordance with the invention, any substitutions at the histidine residue at position 3 will also produce an improved non-metal binding modified albumin because the histidine is a critical aspect of the copper and nickel binding. The preferred substituted modified albumin sequence in accordance with the invention thus has the sequence **Asp-Ala-X**-Lys-Ser-Glu (SEQ ID NO: 4). . ., wherein X represents any amino acid substitution (or insertion or deletion) which will provide steric hindrance or disrupt vital binding interactions sufficient to reduce or eliminate the binding of metals such as copper and nickel to the serum albumin. Because of the critical nature of the histidine at position 3, any amino acid insertions in the leader sequence before this histidine will generally be sufficient to disrupt the metal binding.



clean paragraphs

*Page 15, lines 3-11*:

Addition of the following amino acids to the n-terminus, Glu-Ala-Glu-Phe-**Asp-Ala-His (SEQ ID NO: 5)**, in the recombinant albumin identified as NCP control number A99-13,2393) resulted in greatly reduced coloration of the purified recombinant albumin. This albumin was prepared by conventional recombinant means normally used to obtain albumin from nucleic acids with the nucleic acids being recombined so as to have a sequence coding for the mutated albumin (either directly or through degenerate sequences). The reduction in coloration reflects the reduction in the bound trace metals and was quantitatively demonstrated by the reduction in $A_{400}$ for the albumin of the invention versus normal rHSA when produced and purified under otherwise identical conditions.



clean paragraphs